Claims

1. An adenoviral vector which is defective for replication, capable of being encapsidated in a complementation cell, which is derived from the genome of an adenovirus comprising, from 5' to 3', a 5' ITR, an encapsidation region, an E1A region, an E1B region, an E2 region, an E3 region, an E4 region and a 3' ITR, by deletion of:

(i) all or part of the E1A region and the whole of the portion of the E1B region coding for the early proteins; or

(ii) all or part of the E1A region and all or part of at least one region selected from E2 and E4 regions; or

(iii) all or part of the E1A region and a portion of the encapsidation region.

2. An adenoviral vector as claimed in claim 1, which is derived from the genome of an adenovirus by deletion of all or part of the E1A region and the whole of the portion of the E1B region coding for the early proteins.

3. An adenoviral vector as claimed in claim 2, which is derived, in addition, from the genome of an adenovirus by deletion of all or part of the E3 region.

4. An adenoviral vector as claimed in claim 2 or 3, which is derived, in addition, from the genome of an adenovirus by deletion of all or part of the E2 region.

5. An adenoviral vector as claimed in one of claims 2 to 4, which is derived, in addition, from the genome of an adenovirus by deletion of all or part of the E4 region.

6. An adenoviral vector as claimed in claim 1, which is derived from the genome of an adenovirus by deletion of all or part of the E1A region and all or part of the E2 region.

7. An adenoviral vector as claimed in claim 1, which is derived from the genome of an adenovirus by deletion of all or part of the E1A region and all or part of the E4 region.

8. An adenoviral vector as claimed in claim 6 or 7,

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which is derived, in addition, from the genome of an adenovirus by deletion of all or part of the E1B region.

9. An adenoviral vector as claimed in one of claims 6 to 8, which is derived, in addition, from the genome of an adenovirus by deletion of all or part of the E3 region.

10. An adenoviral vector as claimed in claim 6, 8 or 9, which is derived, in addition, from the genome of an adenovirus by deletion of all or part of the E4 region.

11. An adenoviral vector as claimed in one of claims 3 to 5, 9 or 10, which is derived from the genome of an adenovirus by partial deletion of the E3 region of said genome, while maintaining the portion of said E3 region coding for the gp19kDa protein.

12. An adenoviral vector as claimed in claim 11, in which the portion of the E3 region coding for the gp19kDa protein is placed under the control of elements suitable for the expression of said protein in the host cell.

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13. An adenoviral vector as claimed in one of claims 1 to 12, which is derived from the genome of an adenovirus by deletion of all or part of the E1A region and a portion of the encapsidation region.

14. An adenoviral vector as claimed in claim 13, which is derived from the genome of a human adenovirus type 5 by deletion of the portion of the encapsidation region extending:

(i) from nucleotide 270 to nucleotide 346;

(ii) from nucleotide 184 to nucleotide 273; or

(iii) from nucleotide 287 to nucleotide 358.

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15. An adenoviral vector as claimed in one of claims 1 to 14, which is derived from the genome of an adenovirus selected from canine, avian and human adenoviruses.

16. An adenoviral vector as claimed in claim 15, which is derived from the genome of a human adenovirus type 5.

17. An adenoviral vector as claimed in claim 16, which is derived from the genome of a human adenovirus type 5 by deletion of the portion of E1B region extending

from nucleotide 1634 to nucleotide 4047 at least.

18. An adenoviral vector as claimed in claim 16 or 17, which is derived from the genome of a human adenovirus type 5, in particular by deletion of the portion of the E3 region extending from nucleotide 27871 to nucleotide 30748.

19. An adenoviral vector as claimed in one of claims 16 to 18, which is derived from the genome of a human adenovirus type 5 by deletion of the portion of the E4 region extending from nucleotide 32800 to nucleotide 35826.

20. An adenoviral vector as claimed in one of claims 1 to 19, which is derived from the genome of an adenovirus by deletion of at least 18% of the genome of said virus.

21. An adenoviral vector as claimed in claim 20, which is derived from the genome of an adenovirus by deletion of at least 22% of the genome of said virus.

22. An adenoviral vector as claimed in claim 21, which is derived from the genome of an adenovirus by deletion of at least 40% of the genome of said virus.

23. An adenoviral vector as claimed in claim 22, which is derived from the genome of an adenovirus by deletion of at least 95% of the genome of said virus.

24. An adenoviral vector as claimed in claim 23, which is derived from the genome of an adenovirus by deletion of the whole of the genome of said adenovirus with the exception of the 5' and 3' ITRs and all or part of the encapsidation region.

25. An adenoviral vector as claimed in claim 24, which is derived from the genome of a human adenovirus type 5 by deletion of the portion of the viral genome extending from nucleotides 459 to 35832.

26. An adenoviral vector as claimed in one of claims 1 to 25, which comprises, in addition, an exogenous nucleotide sequence.

27. An adenoviral vector as claimed in claim 26, which comprises, in addition, a gene of interest placed under the control of the elements needed for its

expression.

28. An adenoviral vector as claimed in either of claims 26 and 27, which comprises, in addition, a gene coding for a protein which trans-activates non-adenoviral transcription; said gene being placed under the control of the elements needed for the expression of said protein in a host cell.

29. An adenoviral vector as claimed in claim 28, comprising the gene coding for the *Saccharomyces cerevisiae* Gal4 protein which trans-activates transcription.

30. An adenovirus particle comprising an adenoviral vector as claimed in one of claims 1 to 29.

31. A eukaryotic host cell comprising an adenoviral vector as claimed in one of claims 1 to 29 or an adenovirus particle as claimed in claim 30.

32. A complementation line containing a complementation element, comprising, in particular, a portion of the E1 region of the genome of an adenovirus with the exception of the 5' ITR; said complementation element being capable of complementing *in trans* a defective adenoviral vector and being integrated in the genome of said complementation line or inserted into an expression vector.

33. A complementation line as claimed in claim 32, comprising, in particular:

(i) all or part of the E1A region of the genome of an adenovirus; and

(ii) all or part of at least one region of said genome selected from the E1B, E2 and E4 regions.

34. A complementation line as claimed in claim 32, comprising, in particular:

(i) all or part of the E1A region of the genome of an adenovirus; and

(ii) all or part of at least two of the E1B, E2 and E4 regions of said genome.

35. A complementation line as claimed in claim 32, comprising, in particular:

(i) all or part of the E1A region of the genome of an adenovirus; and

(ii) all or part of the E1B, E2 and E4 regions of said genome.

36. A complementation line as claimed in one of claims 33 to 35, comprising, in particular, all or part of the E1A region and the whole of the E1B region of the genome of an adenovirus coding for the early proteins.

37. A complementation line as claimed in one of claims 32 to 36, comprising, in particular, a portion of the genome of an adenovirus selected from canine, avian and human adenoviruses.

38. A complementation line as claimed in claim 37, comprising, in particular, a portion of the genome of a human adenovirus type 5.

39. A complementation line as claimed in claim 38, comprising, in particular, the portion of the genome of a human adenovirus type 5 extending:

(i) from nucleotide 100 to nucleotide 5297;

(ii) from nucleotide 100 to nucleotide 4034; or

(iii) from nucleotide 505 to nucleotide 4034.

40. A complementation line as claimed in claim 38 or 39, comprising, in particular, the portion of the E4 region of the genome of a human adenovirus type 5 extending from nucleotide 32800 to nucleotide 35826.

41. A complementation line as claimed in claim 38, comprising, in particular, the portion of the genome of a human adenovirus type 5 extending from nucleotide 505 to nucleotide 35826.

42. A complementation line as claimed in one of claims 32 to 41, comprising a portion of E1A region of the genome of an adenovirus lacking its natural promoter; said portion being placed under the control of a suitable promoter.

43. A complementation line as claimed in claim 42, in which said portion of the E1A region is placed under the control of a promoter which is inducible by a protein which trans-activates non-adenoviral transcription.

44. A complementation line as claimed in claim 43, in which said portion of the E1A region is placed under the control of a promoter which is inducible by a protein

which trans-activates transcription encoded by an adenoviral vector as claimed in claim 28 or 29.

45. A complementation line as claimed in claim 43 or 44, in which said portion of the E1A region is placed under the control of a promoter which is inducible by the *Saccharomyces cerevisiae* Gal4 protein which trans-activates transcription.

46. A complementation line as claimed in one of claims 32 to 45, comprising, in addition, a gene coding for a selectable marker.

47. A complementation line as claimed in claim 46, in which the selectable gene codes for puromycin acetyl-transferase.

48. A complementation line as claimed in claim 46 or 47, in which the selectable gene is placed under the control of a promoter which is inducible by a protein which trans-activates transcription encoded by the E1A region of the genome of a wild-type adenovirus, in particular under the control of the promoter of the E2 region of said genome.

49. A complementation line as claimed in one of claims 32 to 48, derived from a cell line which is acceptable from a pharmaceutical standpoint.

50. A complementation line as claimed in claim 49, derived from a cell line selected from the Vero, BHK, A549, MRC5, W138 and CHO lines.

51. A complementation line as claimed in one of claims 32 to 48, derived from a human embryo retinal cell.

52. A method for preparing an adenovirus particle as claimed in claim 30, according to which:

(i) an adenoviral vector as claimed in one of claims 1 to 29 is introduced into a complementation line capable of complementing *in trans* said adenoviral vector to obtain a transfected complementation line;

(ii) said transfected complementation line is cultured under suitable conditions for permitting the production of said adenovirus particle; and

(iii) said adenovirus particle is recovered in the cell culture.

53. A method as claimed in claim 52, according to which a complementation line as claimed in one of claims 32 to 51 is employed.

54. A therapeutic or prophylactic use of an adenoviral vector as claimed in one of claims 1 to 29, an adenovirus particle as claimed in claim 30 or obtained employing a method as claimed in claim 52 or 53, a eukaryotic host cell as claimed in claim 31 or a complementation line as claimed in one of claims 32 to 51.

55. A pharmaceutical composition comprising as therapeutic or prophylactic agent an adenoviral vector as claimed in one of claims 1 to 29, an adenovirus particle as claimed in claim 30 or obtained employing a method as claimed in claim 52 or 53, a eukaryotic cell as claimed in claim 31 or a complementation line as claimed in one of claims 32 to 51, in combination with a vehicle which is acceptable from a pharmaceutical standpoint.